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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,075	09/09/2002	David G. Atkins	ATKINS1	6813

1444 7590 04/17/2007
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WASHINGTON, DC 20001-5303

EXAMINER	
BOWMAN, AMY HUDSON	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/889,075	ATKINS ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-62* is/are pending in the application.

4a) Of the above claim(s) *59-62* is/are withdrawn from consideration.

5)☒ Claim(s) *20-48* is/are allowed.

6)☒ Claim(s) *49-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 2/1/07 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 8/2/06 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 20-62 are pending in the application.

This application contains claims 59-62 that are drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's amendments and/or arguments filed on 2/1/07, with respect to the claim rejections under 35 U.S.C. 112, 2nd paragraph have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, the rejections addressed below are pending.

Sequence Compliance

As explained in the office action mailed on 8/2/06, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this

application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because the disclosure contains sequences which fall under the purview of 37 CFR 1.821 through 1.825 as requiring SEQ ID NOS, but which are not so identified. For example, the drawings contain multiple sequences in excess of 10 nucleotides long that are not identified by a SEQ ID NO. Applicants should be aware that these sequences may not be the only instance necessitating this notice. Applicants should carefully review the application for any further examples of failures to identify any sequences by SEQ ID NO, and to otherwise verify that the application is in compliance. In order to be considered fully responsive, Applicants response to the instant action must put the application into full sequence compliance, as this requirement will not be held in abeyance. Although applicant has filed a new copy of the sequence listing, applicant has not fixed the sequences in the drawings that do not contain proper SEQ ID NOs.

Claim Rejections - 35 USC § 112

Claims 49-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNAzyme-mediated inhibition of EGR-1 expression *in vitro*, does not reasonably provide enablement for DNAzyme-mediated inhibition of EGR-1 expression *in vivo*, or for methods of treating diseases associated with its expression *in vivo*, as explained in the office action mailed on 8/2/2006.

Applicant broadly asserts that it is not understood on what authority the examiner relies in asserting that issues that give rise to unpredictability in the art that apply to antisense oligonucleotides also apply to the use of DNAzymes. As explained in the

office action mailed on 8/2/2006, although the use of DNAzymes is relatively undescribed, the field is well described in regards to the in vitro use of a similar technology, that of antisense oligonucleotides. Accordingly, since the issues that give rise to unpredictability that apply to antisense oligonucleotides also apply to the use of DNAzyme oligonucleotides. The authority that the examiner relies upon is the state of the art. The examiner cited Jen et al. (Stem Cells 2000, Vol. 18, p 307-319) who specifically teaches that "[o]ne of the major limitations for the therapeutic use of AS-ODNs and ribozymes is the problem of delivery.... presently, some success has been achieved in tissue culture, but efficient delivery for in vivo animal studies remains questionable...Given the state of the art, it is perhaps not surprising that effective and efficient clinical translation of the DNAzyme strategy has proven elusive." Jen et al. also teach that "DNAzymes must ultimately overcome the same problems faced by ribozymes and oligonucleotides if they are to be effective in cellular systems" (see first sentence on page 313).

Applicant points to example 1 on page 24 and example 6 on page 31 to conclude that DNAzymes may be successfully administered in vivo with the desired therapeutic effect. It is acknowledged, and was acknowledged in the office action mailed on 8/2/2006 that applicant has demonstrated methods of directly applying the DNAzyme to the desired site surgically or through a stent. Such exemplification is not considered sufficient to overcome the *in vivo* delivery concerns evident throughout the art as cited by the examiner because the means of delivery exemplified by applicant is not consistent with the scope of the instant claims that embrace any type of administration.

The examiner is not disputing that DNAzymes may be successfully administered in vivo in some circumstances but is rather disputing the predictability of being able to deliver the instant DNAzyme in a broad method of administering the DNAzyme and to achieve the desired effect. It is maintained that *in vivo* inhibition of gene expression at the time of filing and even to the present time is not routine for several reasons, primarily due to the problem of delivery, and to a lesser extent, specificity and length of bioactivity. The problem of delivery results from the poor ability of nucleic acid therapeutic to reach the appropriate target cell, and penetrate the membrane (or membranes, since they are typically taken into lysosomes) in sufficient concentrations such that the target gene is inhibited to a degree necessary to result in a therapeutic effect.

The specification as filed does not provide sufficient guidance or appropriate examples that would enable a skilled artisan to use the disclosed compounds or methods of using said compounds in *in vivo* environments, because the specification teaches only prophetic methods of treatment using DNAzyme oligos, or methods comprising direct delivery to the area of injury. The specification does not teach any specific treatment regimen that is specific for any DNAzyme oligonucleotide, but rather relies upon the guidance of the prior art in enabling one of skill to practice the instantly claimed treatment methods.

Allowable Subject Matter

Claims 20-48 are allowed, since the prior art does not teach or suggest making or using DNAzymes targeted to nucleotides 168-332 of EGR-1 of SEQ ID NO: 1.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is (571) 272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy H Bowman
Examiner
Art Unit 1635

AHB

JON E. ANGELL, PH.D.
PRIMARY EXAMINER